

## The PolyPid - A novel local delivery system: from the physic-chemical aspects to innovative and superior therapeutic potential

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**INTRODUCTION:** PolyPid technology is a novel local drug delivery system (DDS) that was planned to control the release of many drugs and biological agents. It was developed in order to fulfill the major deficiencies of the two well established drug delivery systems, polymers and lipids. These deficiencies include a large burst release upon administration and lack of prolonged and controlled drug release necessary to achieve therapeutic efficacy. By synergistically “fusing” the right lipids with the right polymers PolyPid has succeeded to achieve a novel DDS with unmatched performance. This fusion is based on the self assembly of pharmaceutical known polymeric and lipids components into a highly organized nano-scale derived super-molecular structures. The lipids used are mainly synthetic phospholipids and cholesterol. The release rate of the drug can be pre-programmed by the selection of the exact polymer and lipid composition. The PolyPid DDS was characterized by many physical methods including differential scanning calorimetric (DSC), SEM and X-ray diffraction. It was demonstrated that each one of the major component significantly contributing to the final organized structure, and that the drug molecules are fully integrated in the final well organized structure. PolyPid DDS shows a direct correlation between the physic-chemical features of the system and its performance. PolyPid technology platform enables to entrap a large variety of either a single or combination of agent(s) and to release them at a pre-programmed zero-order kinetics rate for the desired time in the preset range of several days to several months. The drugs reservoir is fully protected not only against biological destruction but also against hydration, particularly important when long lasting activity of sensitive drugs is required. This biocompatible and biodegradable family of drug carriers can supply implantable solutions for prolonged and complicated medical protocols. The flexibility of PolyPid solutions allows it to serve as independent structures as well as coating material that can be used with numerous medical devices and implant with a large variety of active materials.

### BonyPid™

The first PolyPid technology based family of products is BonyPid™ which is designed to serve in the orthopedic field. Bones are subject to severe morbidity, and bone infections following orthopedic grafting procedures are common and catastrophic to the patient. Systemic administration of antibiotics is not sufficiently effective due to low penetration to the diseased tissue and the high concentrations needed are not always safely tolerated. Currently available local delivery systems are not sufficiently effective due to high burst and short lasting effect. Consequently, prolonged and controlled local delivery of antibiotics to the bone tissue can play a major role in the treatment of acute and chronic (osteomyelitis) bone infections.

The BonyPid™ is based on the commonly used bio-degradable and biocompatible bone-void-filler particles. These particles are coated with a fine layer of the PolyPid based biodegradable formulation which include a potent antibiotic. Upon in-vivo hydration the entrapped anti-bacterial agent is released over a predefined period and at a pre-set zero order kinetic release rate that was pre-designed to achieve sufficient local drug concentrations. The coating surface is gradually disintegrated layer by layer thereby releasing the antibiotic into the surrounding tissue, while the bone-void-filler scaffold remains and supports bone recovery.

BonyPid™ has been tested pre-clinically in infected rabbit's tibia model. It was clearly demonstrated that the therapeutic efficacy of BonyPid™ is highly effective in both acute and chronic infection models as well as significantly advantageous over the non-formulated free drug.